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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/614,150	07/11/2000	J. CRAIG VENTER	CL000728	1598

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EXAMINER

JOHANNSEN, DIANA B

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 02/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/614,150

Applicant(s)

VENTER ET AL.

Examiner

Diana B. Johannsen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 December 2003.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-16 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 0203.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. It is noted that the Amendment and Response to Restriction Requirement filed July 7, 2003 has been entered. Claims 1, 3-5, 7-9, 11-13, and 15-16 have been amended, and claims 1-16 are pending and under consideration. It is also noted that the computer readable form of the Sequence Listing filed on CD-ROM on December 8, 2003 has been entered.

Priority

2. Regarding applicant's claim for the benefit of provisional application no. 60/157,832, it is noted that the filing date of the application provided in the first line of the specification (as well as in the Oath/Declaration; see below) is incorrect. In order for applicant's priority claim to be proper, the specification must be amended to recite the correct filing date for application no. 60/157,832.

Election/Restriction

3. Applicant's election of the first 1000 transcript sequences provided in the Sequence Listing (i.e., every third sequence beginning with SEQ ID NO: 2 and ending with SEQ ID NO: 3002) in the Response of July 7, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

4. Sequence combination other than the combination set forth in paragraph 3, immediately above, are withdrawn from further consideration pursuant to 37 CFR

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1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the Response of July 7, 2003.

Information Disclosure Statement

5. Regarding the IDS filed February 24, 2003, it is noted that the examiner has modified the 1449 provided by Applicant in order to provide a complete citation for the Search Report of PCT/US01/09231.

Specification

6. The title of the invention is not descriptive of the elected invention. A new title is required that is clearly indicative of the invention to which the claims are directed (i.e., detection reagents and arrays).

Oath/Declaration

7. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because it includes an incorrect filing date for provisional application 60/157,832, and therefore does not fully and correctly identify the application of which benefit is claimed.

Claim Rejections - 35 USC § 101: Non-Statutory Subject Matter

8. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 1, 5, 9, and 13 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

It is noted that the specification does not include any kind of limiting definition of the term "detection reagent," and that the claims as written are therefore sufficiently broad so as to encompass any reagent "capable of detecting" *Drosophila* transcripts as recited in the claims. Thus, the claims encompass, e.g., *Drosophila* genomic nucleic acids as they exist in nature, as such genomic nucleic acids may be employed as a "detection reagent" in detecting the transcripts of the claims. Claims 1, 5, 9, and 13, as written, do not sufficiently distinguish over detection reagents that exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by amending the claims to require the presence of a structural feature or property that is not naturally-occurring. See also MPEP 2105.

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph: Utility

10. The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

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"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

11. Claims 1-16 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

It is noted that this rejection applies to the claims to the extent that they are drawn to the predicted transcript sequences elected by Applicant.

The claimed subject matter is not supported by a specific, substantial, and credible asserted utility because the disclosed uses are generally applicable to broad classes of this subject matter. Further characterization of the claimed subject matter would be required to identify or reasonably confirm a "real world" use.

The specification teaches that the detection reagents and arrays of Applicant's invention comprise "one or more fragments of the *Drosophila melanogaster* genome of the present invention, particularly ORFs" (see page 4), and further teaches that the SEQ ID Nos of the elected invention are "predicted transcript sequences" (see, e.g., page 3). The specification asserts that the claimed invention "can be used to track the expression of many genes" (see page 4) and that it may be used "to measure the absence, presence, and amount of hybridization" for all sequences simultaneously, thereby obtaining data "for large scale correlation studies on the sequences, expression patterns, mutations, variants, or polymorphisms among samples" (page 16). These

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uses asserted in the specification are general utilities and uses in further research that are applicable to virtually any group of predicted transcripts or predicted ORFs. For example, any group of predicted ORF sequences could be employed in the study of expression patterns and/or the study of "mutations, variants, or polymorphisms among samples." While such experiments might eventually result in the identification of, e.g., a particular expression pattern or set of sequences or polymorphisms associated with a particular condition or genetic defect, such general research methods do not constitute substantial uses that are specific to the group of molecules claimed by applicant. The sequences elected by Applicant appear to constitute a group of the first 1000 predicted transcripts identified in the *D. melanogaster* genome, rather than, e.g., a specific group of actual transcripts associated with (and thereby useful in detecting) a specific condition or state. Therefore, not only would further experimentation be required to establish some type of specific use for this group of sequences (if such a use even exists), but additional research would be required to establish that this group of sequences are actually transcribed in the manner predicted by Applicant. Again, further research and experimentation on nucleic acids or a group thereof constitutes a general utility, rather than a specific and substantial "real world" use. See *Brenner v. Manson*, 383 U.S. 519, 535-536, 148 USPQ 689, 696 (1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion". A patent is therefore not a license to experiment with the objective of eventually identifying a specific and substantial use for a product. As the specification does not provide any evidence of a specific and substantial use for the elected

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invention, the claimed invention is not supported by a specific, substantial and credible asserted utility.

With regard to the possibility that there may exist a well-established utility for the claimed invention, it is noted that the prior art does disclose useful arrays that, because of the broad and indefinite language of the instant claims, are encompassed by the claims as presently written. However, to the extent that the claims are drawn to the particular sequences elected by Applicant, the prior art does not disclose any type of specific use for this group of predicted transcripts. Thus, the prior art does not provide any evidence of a well-established utility for the elected invention.

Applicant should explicitly identify a specific, substantial, and credible utility for the claimed invention and establish a probative relation between any evidence of record and the originally disclosed properties of the claimed invention.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-16 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, second paragraph

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-16 are indefinite over the recitation of the limitation “capable of detecting” in claims 1, 5, 9, and 13. Capability is a latent characteristic, and any reagent may be “capable of detecting” nucleic acids under appropriate conditions and/or after sufficient modification, etc. It is not clear how one might differentiate reagents that are “capable of detecting” *Drosophila* transcripts from any other reagents. Further, it is not clear whether the claims actually require reagents that, e.g., specifically detect *Drosophila* transcripts, or whether the “capable of detecting” limitation permits the claims to encompass any reagent meeting the other limitations (if any) recited therein. Accordingly, the claims are vague and indefinite.

Claims 1-16 are indefinite over the recitation of the phrase “wherein each of at least” 1000/2000/5000/10,000 “of said *Drosophila* transcripts consists of a nucleotide sequence selected from the group consisting of...” in claims 1, 5, 9, and 13, respectively. It is unclear from this language as to whether the claims encompass reagents that are “capable of detecting” at least 1000/2000/5000/10,000 copies of the same transcript, or whether the claims require a reagent that is “capable of detecting” at least 1000/2000/5000/10,000 different transcripts selected from the recited molecules. Clarification is required.

Claims 1-16 are indefinite over the recitation of the phrase “the transcript sequences of SEQ ID NOS:2, 5, 8, 11....43001, 43004, 43007” in claims 1, 5, 9, and 13.

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It is unclear from this language as to whether the claims require the particular sequences set forth in the recited SEQ ID Nos (i.e., the full length of SEQ ID NO: 2, the full length of SEQ ID NO: 5, etc.), or whether the claims encompass subsequences of the recited SEQ ID Nos that constitute "the transcript sequences" of those recited SEQ ID Nos. Clarification is required.

Claims 1-16 are indefinite over the recitation of the limitation "SEQ ID NOS:2, 5, 8, 11...43001, 43004, 43007" in claims 1, 5, 9, and 13. This recitation does not make clear which particular sequences are encompassed by the claims. Accordingly, the claims are vague and indefinite.

Claims 3-4, 7-8, 11-12, and 15-16 are indefinite over the recitation of the phrase "wherein said array is comprised of...". It is unclear whether this language requires an array that is constructed from ("comprised of") oligonucleotides/polynucleotides, or whether the claims are intended to encompass an array that comprises oligonucleotides/polynucleotides.

Claims 3-4, 7-8, 11-12, and 15-16 are indefinite over the recitation of the phrase "wherein each of said" oligonucleotides/polynucleotides "is fully complementary to one of said Drosophila transcripts." Again, it is unclear whether the claims require an array comprising multiple copies of a single oligonucleotide/polynucleotide that is "fully complementary to one" of the multitude of previously recited transcripts, or whether the claims are intended to encompass multiple different oligonucleotides/polynucleotides, each of which is fully complementary to a different one of the recited transcripts. It is further noted that the claims previously refer to both a group of 1000/2000/5000/10,000

"or more *Drosophila* transcripts" and to a subset of "at least" 1000/2000/5000/10,000 of said transcripts, and it is not clear which of these groups constitutes "said *Drosophila* transcripts" as recited in claims 3-4, 7-8, 11-12, and 15-16.

Claim 16 is indefinite because it is unclear as to whether the claim is intended to be drawn to an array that "is comprised of" polynucleotides "from about 100 to about 1000 nucleotides in length," as recited in the claim, or to an array that comprises (or additionally comprises) "short oligonucleotides from about 5 to about 100 nucleotides in length," as recited in claim 15, from which claim 16 depends. It appears that claim 16 may have been intended to depend from claim 14, rather than claim 15.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 1-3, 5-7, 9-11, and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (U.S. Patent No. 5,474,796 A [12/1995]).

Brennan discloses an array of oligonucleotides comprising all possible 10-mers (see entire reference, particularly Example 4). It is an inherent property of Brennan's array that it is "capable of detecting" any or all of the transcripts and related molecules encompassed by the claims, as the array could be employed in sequencing any of the recited molecules. Regarding claims 3, 7, 11, and 15, it is noted that as the array of Brennan comprises all possible 10-mers, it includes oligonucleotides "from about 5 to

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about 100 nucleotides in length” that are “fully complementary to one of said *Drosophila* transcripts.”

18. Claims 1-2, 5-6, 9-10, and 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Bryant et al (Proceedings of the National Academy of Sciences USA 96:5559-5564 [5/1999]).

It is noted that the instant application claims priority to several provisional applications, three of which (60/161,932, 60/173,383, and 60/191,637) contained a complying computer readable Sequence Listing for purposes of comparison with the instant application. Those applications do not provide basis for the group of sequences claimed by applicant herein, and given the multitude of sequences disclosed in the remaining provisional applications and encompassed by the instant claims, the examiner was unable to determine by visual inspection whether those applications provide basis for the claimed invention. Accordingly, at the present time, the effective filing date of the instant application is considered to be July 11, 2000. Applicant is requested to specifically identify in which provisional application or applications basis for the claimed invention may be found. If it is established that applicant is entitled to an earlier effective filing date corresponding to filing dates of one of the named provisional applications, the instant rejection will be applicable under 35 U.S.C. 102(a).

It is noted that the claims as written are sufficiently broad so as to encompass microarrays that are “capable of detecting” one of the claimed nucleotide sequences in any manner or by any type of method, etc. Bryant et al disclose a microarray comprising “4,500 unique *Drosophila* cDNAs” (page 5560, left column). It is an inherent

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property of the microarray taught by Bryant et al that it is "capable of detecting" any number of Drosophila transcripts (1000, 2000, 5000, 10,000, etc.), wherein each of those transcripts "consists of a nucleotide sequence" selected from among those elected by applicant (including complements and RNA equivalents). Accordingly, Bryant et al anticipate the claimed invention.

Conclusion

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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A handwritten signature in black ink, appearing to read "Diana B. Johannsen", followed by a long horizontal line extending to the right.

Diana B. Johannsen
Patent Examiner
February 19, 2004